Hypothyroidism and protein-losing enteropathy: A case report

Hipotiroidismo y enteropatía pierde-proteínas: a propósito de un caso

We report the case of a 34-year-old female patient with a history of hypothyroidism, lymphangiectasia, and protein-losing enteropathy on treatment with levothyroxine (200 μg/day) who attended the emergency room complaining of dyspnea and fever. A chest X-ray showed bilateral pleural effusion and enlarged cardiac silhouettte, while echocardiography revealed pericardial effusion with systolic-diastolic collapse of the right chambers. The results of laboratory tests performed were as follows: TSH, 21.3 U/mL (normal: 0.4–4); free thyroxine, 0.69 μg/dL (normal: 0.8–1.8); triiodothyronine, 0.62 pg/mL (normal: 2–4.4); serum albumin, 17.9 g/L (normal: 34–48); prealbumin, 11.4 mg/dL (normal: 20–40); total cholesterol, 118 mg/dL (normal: 150–200); triglycerides, 100 mg/dL (normal: 50–200); vitamin E 1.9 μg/mL (normal: 5–20) (corrected for cholesterol and triglyceride levels of 0.89 mg/g, in the lower limit of normal: normal: >0.8 mg/g); vitamin A, 0.09 mg/L (normal: 0.3–1); 25-OH vitamin D, <9 ng/mL; copper, 70 μg/dL (normal: 80–155); zinc 56 μg/dL (normal: 68–107); and serum selenium, 44 μg/dL (normal: 60–120).

Multifactorial pleural and pericardial effusion in the setting of hypoproteinemia and hypothyroidism, with respiratory tract superinfection, was diagnosed, and was treated with evacuating pericardiocentesis, oxygen therapy, and intravenous ceftriaxone. Her weight during hospitalization was 70 kg, and a low-fat diet was started (20–30 g of lipids during her hospital stay), together with oral supplements to provide a total of 600 kcal/day, with 27 g of hydrolyzed protein and 22 g of lipids, of which 15.4 g were medium-chain triglycerides (MCTs). Thirty grams of oil with MCTs and supplements of vitamin A (50,000 IU/day), E (200 mg/24 h), and D (10,000 IU/week) were also added. Copper and zinc levels were considered moderately low in the context of the acute phase, and watchful waiting was decided upon. The patient reported good compliance with levothyroxine treatment, and low drug levels despite very high doses (approximately 2.8 μg/kg/day) were therefore attributed to the underlying gastrointestinal disease. The dose was increased to 250 μg/day. Some days later, the patient experienced a clinical improvement with decreased stool count and steatorrhea and was discharged.

At an outpatient monitoring visit at three months, her clinical condition was much improved. She weighed 70.3 kg and reported a lower number of stools, with mild steatorrhea. She was still taking oral supplements, and laboratory tests showed an improvement in the nutritional parameters: prealbumin 18 mg/dL and albumin 27.2 g/L. Levels of copper 88 μg/dL, serum selenium 60 μg/L, vitamin A 0.5 mg/L, and vitamin E 2.9 μg/mL (corrected: 1.4 μg/g) were normalized. The zinc level was 59 μg/dL, and her vitamin D level continued to be less than 9 ng/mL despite supplementation. Thyroid hormone levels had normalized (TSH 2.27 μU/mL and free thyroxine 1.1 ng/dL).

A review of the patient’s clinical history during her hospitalization found that she was born with congenital lymphedema and intestinal lymphangiectasia that required surgery several times during childhood. However, she was not diagnosed with Hennekam syndrome until she was 28, based on dysmorphic signs and the delayed development of her daughter. Previously, at the age of 24, she had experienced pleuropericarditis in the context of myxedema with 226 μU/mL of TSH and 0.06 ng/dL of free T4. Subsequently, patient monitoring was irregular, but the levothyroxine dose was increased to 200 μg/day, due to the difficulty in normalizing TSH.

Hennekam syndrome is an extremely uncommon cause of hypothyroidism characterized by congenital lymphedema, mainly affecting the limbs and genitalia, and developmental delay. It is also related to dysmorphic traits (flattened face, broad and flattened nasal bridge, and hypertelorism), glaucoma, hypacusis, and dental and renal abnormalities. It is characterized by lymphangiectasia in the bowel, pleura, pericardium, thyroid gland, and kidney. An intestinal biopsy shows a dilation of lymphatic vessels in the lamina propria that leads to protein-losing enteropathy and malabsorption. Thyroid lymphangiectasia is the cause of hypothyroidism.\(^\text{1-5}\)

This genetic condition was described by Hennekam in 1989.\(^\text{1}\)

To our knowledge, 36 cases have been reported worldwide.
Transient electrocardiographic abnormalities during hypoglycemia

Alteraciones electrocardiográficas transitorias durante un episodio de hipoglucemia

Hypoglycemia, defined as plasma glucose levels <70 mg/dL, is a potentially serious complication occurring in 40% of patients with type 1 diabetes mellitus, and less commonly in patients with type 2 diabetes mellitus. Different changes in the electrocardiogram (ECG) associated with hypoglycemia have been reported.

The case of a female patient referred to the emergency room of our hospital for loss of consciousness is reported below. This was a 74-year-old woman with long-standing diabetes on treatment with metformin 850 mg/12 h and Lantus® insulin 30 IU at dinner. She was also being treated with pravastatin 10 mg and Eutirox® 50 μg for dyslipidemia and hypothyroidism respectively. At admission, the patient was unconscious, with no response to verbal or painful stimuli and mydriatic, nonreactive pupils. She was breathing spontaneously. Her blood pressure was 110/75 mmHg, and heart rate 56 bpm. Heart auscultation revealed cardiac rhythmic sounds, with no murmurs, and pulmonary auscultation found no pathological sounds. The initial capillary blood glucose level was 35 mg/dL. Intravenous infusion of hypertonic glucose resulted in the recovery of consciousness and increased the blood glucose level to 280 mg/dL. Laboratory test results included: chemistry: urea, 49 mg/dL; creatinine, 1.2 mg/dL; sodium, 141 mEq/L; potassium, 3.9 mEq/L; chloride, 112 mEq/L; troponin Ic (peak value), 2.1 μg/dL; baseline arterial blood gases: pH 7.42, pCO₂ 35 mmHg, pO₂ 75 mmHg, HCO₃⁻ 22 mmol/L; complete blood count: WBCs, 8760/μL; hemoglobin, 11.8 g/dL; and platelets, 316,000/μL. The ECG at admission (Fig. 1) showed sinus rhythm at 62 bpm with signs of left ventricular hypertrophy, 1 mm ST segment elevation in aVR, and 1 mm ST segment depression in I, aVl, aVf, and V4–V6 with generalized asymmetrical negative T waves, and a QTc interval of 510 ms. The ECG performed after the correction of hypoglycemia with intravenous hypertonic

To date, this is the first case reported in Spain. Twenty-five percent of patients have autosomal recessive mutations in the CCBE1 gene, and more than 20% in the FAT4 gene. CCBE1 is a key gene for the development of lymphatic system. However, the relationship with FAT4 has not yet been elucidated. Other genes involved include VEGFR3 and GJC2. In this patient, diagnosis was initially based on the clinical history and phenotype.

Hypothyroidism occurring in this syndrome is difficult to manage due to decreased levothyroxine absorption secondary to intestinal lymphangiectasia, which may require very high thyroid hormone doses. The treatment of malabsorption syndromes depends on symptom severity. It usually consists of a low-fat, protein- and mCT-rich diet, in addition to supplements of lipid soluble vitamins and electrolytes. Home enteral nutrition by mouth or tube using products specifically designed for malabsorption syndromes (with fat mainly as mCTs and partially hydrolyzed protein) may sometimes be required. Subcutaneous octreotide treatment or parenteral nutrition may be required in very severe cases. If pleural or pericardial effusion occurs, drainage may be needed. Lymphedema may be very disabling, requiring surgery and diuretics. Its prognosis is highly variable, and if severe complications occur, life expectancy may be decreased. Differential diagnosis includes other syndromes causing congenital lymphedema such as Noonan syndrome, Aagenes cholestasis-lymphedema syndrome, Milroy’s disease, or Turner syndrome.

In conclusion, Hennekam syndrome is a rare cause of hypothyroidism and intestinal malabsorption secondary to lymphangiectasia that requires adequate nutritional treatment with low-fat diet, protein supplementation, and deficient lipid soluble vitamins, and careful, possibly high levothyroxine dosage.

Conflicts of interest

The authors state that they have no conflicts of interest.

References


Irene Berges-Raso*, Ismael Capel, Assumpta Caixàs, Roser Trallero, Mercedes Rigla

Servicio de Endocrinología y Nutrición, Hospital Universitario Parc Taulí, Sabadell, Barcelona, Spain

*Corresponding author.
E-mail address: inberges@tauli.cat (I. Berges-Raso).